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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/281,528 03/30/99 ROBERTSON

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EXAMINER

BRABIK, C.

ART UNIT

PAPER NUMBER

1633

DATE MAILED:

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/281,528

Applicant(s)

ROBERTSON, DOMINIQUE

Examiner

Christopher Drabik

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 September 2000.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 22-33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-21 and 31-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

Detailed Action

Applicants election with traverse of Group I, claims 1-21 and 31-34, in paper # 10 is acknowledged. The traversal is on the grounds that it would not be an undue burden to examine the claims of Groups I –III concurrently. This is found to be unpersuasive because of the significant divergence of subject matter encompassed by the three groups. The elected Group (I) contains claims to a geminivirus comprising heterologous DNA with the claimed capability of silencing genes. Group II claims a silencing vector comprising the geminivirus genome, origin of replication and heterologous DNA. These groups are divergent because of the different structures and functions circumscribed by the claims. And, hence, would require a significant increase in the area of subject matter searched. Group III diverges from the subject matter of II and III in that the claims of Group III are drawn to a method of screening plants. The method claims of Group III clearly includes subject matter not anticipated by the claims of Groups I and II. Therefore it is maintained that the inventions of Group I, II and III are distinct and appropriately classified and searched separately.

The requirement is still deemed proper and is therefore made **FINAL**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-21, 31 -34 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification provides adequate description for the construction and use of a geminivirus based vector capable of silencing two genes in *N. benthamiana*: the methyl transferase gene and a transgene, luciferase. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with **sufficient relevant identifying characteristics** (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention Pfaff v. Wells Electronics, Inc 48 USPQ2d 1641, 1646 (1998). The claimed invention encompasses sequences capable of silencing any all genes in any and all plants. The inventors provide specific sequences used for silencing the *N. benthamiana* methyl transferase gene and transgenic luciferase gene, but no direction is given as to identify what sequences in other genes are claimed as capable of silencing said genes. (would be required to achieve the same effect.) Hence the applicants claim a genus of sequences, with only the description of two species of sequences within that genus.

Claims 1 and 12 incorporate the language "DNA having substantial sequence similarity to a gene endogenous to a plant", however, no guidance is given as to how one skilled in the art might determine these sequences. For example, the claim encompasses sequences with 1% homology to an "endogenous gene". This can mean 2

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or 3 base pairs adjacent to each other. Further, the applicants define "endogenous gene" as encompassing transgenes. This means any and all sequences which might be inserted into a plant genome including, but not limited to, any and all genes from viruses, prokaryotes and eukaryotes. It should be noted that genes termed "endogenous" can also mean those derived from a geminivirus if the vector virus is a different species (or even a different strain or subtype) than the virus from which the transgene is derived. The applicants clearly fail to provide evidence for having or knowing the two or three nucleotides required to silence any and all genes. It is, therefore, deemed that the inventors fail to convincingly prove that at the time of application they were in possession of the claimed invention.

Claims 2-11 and 31-34 depend upon claim 1 and are therefore subject to the limitations of claim 1. Claims 13-21 and 31-34 depend upon claim 12 and are subject to the limitations of claim 12. Since it is apparent that the applicants are not in possession of the inventions of claim 1 and 12, it is appropriate to reject all dependent claims. Hence, claims 2-11, 13-21 and 31-34 are rejected under 35 USC 112 paragraph 1

Claim 31-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the silencing of the methyl transferase gene and the luciferase gene in *N. benthamiana*, does not reasonably provide enablement for the silencing of any and all genes in any and all plant species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Gene silencing in plants as a phenomenon has long been recognized. Silencing has been shown to occur in endogenous genes, transgenes and viral genes. Several mechanisms have been suggested to explain how gene silencing in plants occur. They include events at the transcriptional and post-transcriptional level. The state of the art is such that silencing is as yet incompletely understood. Thus Covey explains: "Although some aspects of gene silencing are becoming better understood, little is as yet known about the relationship between nuclear and cytoplasmic events." (see Abstract in Covey SN et al (2000) Plant Molecular Biology, 43: 307-322) The unpredictability of transgene silencing has been noted by Neuhuber et al. They state: "Although the basic phenomenon of homology-dependent gene silencing has been well established, a number of questions in addition to those concerning mechanistic details remain. One of these is why some genes escape inactivation despite the presence of a homologous partner....Even in the cases where the presence of a transgene can lead to the inactivation of a homologous partner, this happens only in a subset of transformants in which both the transgene and homologous resident (trans)gene continue to be expressed." Admittedly, the invention of the instant application involves an episome, which is different from an integrated transgene, however, it is possible that the two forms of silencing share commonalties. The fact that transgene silencing is incompletely predictable reflects upon the level of confidence involved in episomally mediating gene silencing.

Little precedent for gene silencing using episomes as demonstrated by the applicant exists in the literature. One significant example is the use of a gemini virus

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based vector to silence the chalcone synthase gene of *P.hybrida*. Atkinson et al was able to illustrate that the production of episomes from an integrated copy of a geminiviral based gene construct was capable of silencing a desired gene. (Atkinson et al (1998) The Plant Journal Post 15 (5) 593-604) Silencing, however, was not uniform in all plants and a correlation between episomal copy number and the degree of silencing could be drawn. The inventor of the instant application has contributed to an article describing essentially the claims addressed herein. (Kjemtrup et al (1998) The Plant Journal 14(1):91-100) The authors appear to hold that episomal gene silencing is as yet uncertain. They state there study is undertaken... "To **begin** to understand the relationship between episomal DNA and gene silencing, we sought to determine if silencing nuclear genes could be triggered by homologous sequences carried by a geminivirus episome" (examiners emphasis). The authors provide evidence that they can down-regulate the expression of two genes, but they plainly state that there application of a geminivirus based vector to episomally silence a gene is a new area of endeavor.

It is further noted that claim 32 is drawn to "A plant comprising a plurality of cells..." Plurality in this context can mean two or several cells. These cells could be widely distributed in the plant. The claims as a whole are drawn to silencing genes in a plant. It is questioned whether down regulating one gene in several cells widely distributed in a plant constitutes silencing. Hence, the silencing of a gene in a plurality of cells does not enable the claim of silencing of genes in a plant.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-21 and 33-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is also noted that claim 1 appears to be an incomplete claim. The preamble of the claim describes "A geminivirus silencing vector." . The body of the claim, however, does not substantiate that the geminivirus of the preamble is capable of supporting the assertion that any and all genes can be silenced by said vector.

The term "substantial" in claims 1, 8, 9, 12, 18 and 19 is a relative term which renders the claim indefinite. The term "substantial" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. As described above, the term substantial has little definite meaning when describing the homology of two gene sequences. Any given DNA sequence has at least 1% homology with a plurality of possible genes. The claims, therefore, do not specifically point out the sequences present in said "silencing vector" which applicants mean to claim.

Claims 2-11 and 31-34 depend upon claim 1 and are therefore subject to the limitations of claim 1. Claims 13-21 and 31-34 depend upon claim 12 and are subject to the limitations of claim 12. Because the term "substantial" in claim 1 and 12 is vague

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and indefinite, it is appropriate to reject all dependent claims. Hence, claims 2-11, 13-21 and 31-34 are rejected under 35 USC 112 paragraph 2

Claim 1,6-9,12,16-19 and 21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "heterologous" in claim 1,6-9,12,16-19 and 21 is a relative term which renders the claim indefinite. The term "heterologous" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Heterologous is a relative term which could mean a plurality of possible nucleic acid sequences in regard to a reference sequence. Heterology encompasses, non-exclusively, a single base difference, multiple base differences, a rearrangement of sequence, DNA with modified bases and/or bases not included in the set adenine guanine, cytosine and thymine. Combinations of these possibilities can also be (envisioned) considered as heterologous to a reference sequence. Applicants define heterologous DNA as "DNA that is not naturally found in conjunction with the DNA episomal construct, i.e. that has been introduced by genetic engineering techniques." (p11 lines 8-10) This disclosure does not further allow one skilled in the art to distinguish a claimed subset of sequences from an infinitely large set of possibilities as set forth in a limited example above.

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Claims 2-11 and 31-34 depend upon claim 1 and are therefore subject to the limitations of claim 1. Claims 13-21 and 31-34 depend upon claim 12 and are subject to the limitations of claim 12. Because the term "heterologous" in claim 1 and 12 is vague and indefinite, it is appropriate to reject all dependent claims. Hence, claims 2-11, 13-21 and 31-34 are rejected under 35 USC 112 paragraph 2.

Claim 11 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "observable" in claim 11 is a relative term which renders the claim indefinite. The term "observable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. A phenotypic trait can be considered as any manifestation of a gene. The term "observable" in regards to a phenotypic trait is not clearly defined by the applicant because the mode or degree of experimentation required to view a phenotypic trait is not provided. A phenotypic trait can be the color of a plant. It also might mean the transcription of an RNA molecule or the translation of a protein molecule. The applicants do not provide guidance as to what they consider as an observable trait and therefore the claim is rendered vague and indefinite.

Claims 1-21 and 31-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "endogenous gene" in claims 1, 4,8,9,12,14,18 and 19 is used by the claim to mean "a gene integrated into the chromosomal DNA of the plant gene. (p10 lines 3 and 4" while the accepted meaning is "wild type and transgenes."

The definition for endogenous gene as set forth by the applicants is vague, indefinite and, somewhat confusing. The definition in the specifications states that for a gene to be considered endogenous it must be integrated into a gene. This means that for purposes of the instant application only genes within other genes are claimed as targets of gene silencing. It is suggested by the examiner that applicants mean 'genes integrated into the chromosomal DNA of the plant **genome**.

In addition, the commonly accepted definition for an endogenous gene is a gene which naturally occurs in a plant i.e. the gene has not been introduced by means of laboratory transformation techniques. The definition of endogenous gene used by applicants is vague and indefinite because it encompasses essentially all genes, since, in theory, any given DNA sequence could be introduced into the genome of a plant. Because the applicant fails to distinctly point out which genes the invention encompasses it is appropriate to reject claims under 35 USC 112 paragraph 2.

Claim 4,5 and 17-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 5 recite the limitation "a DNA construct..." in reference to claim 3 . There is insufficient antecedent basis for this limitation in the claim. Claims 4 and 5 are drawn to a DNA construct which improperly refers to a vector recited in claim 1. The term DNA construct has a decidedly different meaning then the term vector. It is widely accepted in the field that "vector" specifically refers to the use of a DNA construct to transfer DNA into cells. The term DNA construct used alone as in claims 3 and 4 do not have the same restricted definition in meaning and, hence, it is not clear what the applicants mean to claim.

The term vector recited in claims 17-21 has no antecedent basis in the claim which they depend upon. Claim 17 – 21 depends upon claim 12. Claim 12 recites " A DNA construct comprising a geminivirus genome,..." This claim has no implication for the use of said DNA construct within the context of a cell. The term "vector" in claims 17-21 imply the transfer of nucleic acid into a cell. These dependent claims do not further limit the claim which they depend upon, but, rather, increase the scope of the independent claim. Claims 17-21, therefore do not appropriately point out what the applicants mean to claim. ***It should be further noted that since it is not inferred that claim 12 involves an in vivo use for the DNA construct, this claim does not encompass any use regarding the silencing of genes.***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office

action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1-9,11-16, 18,19, 21, 31 and 32 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Matzeit et al. (Matzeit, V et al (1991) The Plant Cell 3: 247-258)

Claims 1-7 are based on a vector comprising the geminivirus genome which has heterologous DNA inserted. The said heterologous DNA is described as “having substantial similarity to a gene endogenous to a plant,” In the specification the applicant further describes that an endogenous gene “...include(s) those that occur naturally in the plant genome, as well as those artificially introduced.” (page 10, lines 3-7) Thus an endogenous gene can be considered a plurality of possible, eukaryotic, prokaryotic or viral DNA sequences, with no limitations except that the sequence must be present in a plant. Claims 12-16, 18 and 19 essentially reiterate 1-7, maintaining the same open description of an endogenous plant gene.

The introduction of antibiotic resistance genes derived from e.g. bacteria has commonly been used in the plant sciences for the generation of stable transgenic plant cells. For example, the neomycin phosphotransferase gene has been inserted into a

variety of plant cells including maize (Fromm, ME et al (1986) Nature 319:791-93) and tobacco (Paszkowski J et al (1992) Plant Molecular Biology 19:825-836). The neomycin gene has also been used to stably transform cell lines within the context of tomato golden mosaic virus (TGMV). (Hayes et al (1988) Nature 334: 179-182). In Hayes' disclosure, the coat protein of TGMV is replaced with the neo gene and expression of the gene driven by the TGMV promoter normally associated with coat protein coding sequence.

Matzeit et al describe the experiments using the geminivirus white dwarf virus (WDV). In there experiments they delete the gene encoding the coat protein and insert the neomycin phosphotransferase gene. Since it has been established that plant cells are commonly transformed with genes such as the neomycin transferase gene and since this gene can be considered endogenous to a plant based on the definition set forth by the applicant, the vector of Matzeit clearly anticipates claims 1, 2, 6, 8, 9, 12, 16, 18, and 19.

The vector described by Matzeit includes a promoter opearebly associated with the inserted heterologous DNA. The promoter is the geminivirus coat protein promoter. And hence the claims of 2, 3, 13, and 15 are clearly anticipated by Matzeit. In addition, it has been demonstrated by Hayes et al that a plant cell containing an endogenous gene can be associated with the geminivirus coat protein promoter. Hence, the coat protein promoter included in Matzeits' construct can also be considered a promoter present in vivo as a substituent of an endogenous gene and, therefore, claims 4 and 14 are clearly anticipated by Matzeit.

It should be further noted that Stanley et al discloses the construction of pseudorecombinant African cassava mosaic viruses in which the coat protein of the Kenyan and Nigerian isolates have been exchanged. (Stanley et al (1985) 66:1055-1061) Within the scope of the definition of "heterologous DNA" and "endogenous gene" used by applicant these constructs also clearly anticipate claims 1-9,11-16, 18,19, 21, 31 and 32 set forth in this rejection. In particular, Stanley's constructs clearly anticipate claim 10.


Conclusion

No claim contained in the restricted set examined herein is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Drabik whose telephone number is 703-605-1156. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 703-305- 4051. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234. Questions regarding review of formality issues may be directed to Kim Davis, the patent analyst assisting in this application. She may be reached at 703-308-4242.


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